## REMARKS

In this response to the Office Action dated September 24, 2008, claims 1, 7, 9, 11-13, 15, 19, 20, and 26-35 are amended to further clarify the claimed subject matter. Claims 36 and 37 are newly added and support for these claims can be found from, for example, claims 1 and 15 as originally filed. Claims 38 and 39 are also newly added. Support for these new claims can be found in Figure 12, in which a 5' untranslated region (5'UTR) from +1 to +90, and ending with the ATG translation-initiation codon is shown in gray. This region corresponds to nucleotides 2384-2473 in SEQ ID NO:3. Claims 22-24 are canceled without prejudice. No new matter has been added. Claims 1, 7, 9, 11-15, 19-21, and 26-39 are currently pending in the application. In view of the amendments and comments as set forth herein, Applicants respectively request reconsideration and withdrawal of the claim rejections.

**Objection to Claims**

In the Office Action, the Examiner set forth objections to claims 1, 7, 9, 11-13, 15, 20 and 26-35. In reply, Applicants have amended the claims as follows:

The article "an" has been inserted prior to "operably linked sequence" in claims 1 and 7.

The preposition "of" after the word "residues" has been deleted in claims 1, 7, 15, and 26-35.

Some recitations in claims 1, 7 and 15 that include the language "native form" has been deleted.

In claim 7, "the method" has been replaced with "a method", an article "a" has been inserted prior to "portion thereof", and an amendment so that the claim includes the recitation "--a structural gene or other nucleic acid; wherein the promoter is obtainable by a method of isolating a genomic DNA or a portion thereof from plant cells, rendering the genomic DNA or the portion thereof single stranded and then hybridizing to the genomic DNA or the portion thereof a primer--".

Claim 9 is now dependent from claim 1.

Claim 12 has been rewritten to recite "wherein the structural gene or other nucleic acid is operably linked to said promoter".

In claim 13, the article "a" has been replaced with "the" prior to "plant", the recitation of "regulatory gene" has been placed with "the other nucleic acid", the recitation of "facilitate the altering" has been replace with "alters". In addition, the recitation of "--the other nucleic acid which then alters the plant characteristic." has been added.

In claim 20, the article "a" has been inserted prior to "reproductive portion".

In light of the foregoing amendments, Applicants respectively request withdrawal of the objections to claims.

**Rejection of Claims 1, 7, 9, 11-15 and 19-24 under 35 U.S.C. 112, first paragraph**

In the Office Action, the Examiner rejected claims 1, 7, 9, 11-15 and 19-24 under 35 U.S.C. § 112, first paragraph as allegedly failing to provide enablement for some embodiments. Applicants respectively traverse these rejections as set forth below.

The independent claims 1, 7 and 15 relate generally to a promoter comprising any one of: **(i)** a sequence of nucleotides having the sequence set forth in SEQ ID NO:3; **(ii)** a fragment of (i) wherein said fragment comprises residues 2298 to 2384 of SEQ ID NO:3; **(iii)** a sequence of nucleotides with at least 95% identity to the sequence of nucleotides of (ii); or **(iv)** a sequence of nucleotides complementary to anyone of (i), (ii) or (iii).

In the Office Action, the Examiner cited that the subject matters of claims 1, 7, and 15 for a sequence set forth in (i) and (ii) are enabling. *See* page 4 of the Office Action. With the amendment herein, the fragment recited in (ii) has been amended from 368 bp of "the nucleotide residues 2016 to 2384" to 86 bp of "the nucleotide residues 2298 to 2384". Like the 368 bp fragment, the nucleotide sequence of the 86 bp and its activity in multiple plant tissues are disclosed in the specification. In particular, Figure 11 of the present application shows that all of the promoters including this 86bp region have been expressly described in the specification as active. Therefore, the claimed matters related to the 86 bp fragment of (ii) are fully enabled by the specification.

The Examiner, however, alleged that the enablement for the subject matters for a sequence cited in (iii) or (iv) is not reasonably provided in the specification. More particularly, the Examiner contended that the specification does not disclose "the required structural aspects of the sequences" to provide the promoter function. In the office action, these required structural

aspects appear to indicate one or more nucleotide that can cause the decline in the promoter activity if mutated. The Examiner asserted that promoters comprise critical regions and, therefore, without knowing such critical sequences, it is impossible for a skilled person in the art to determine a series of sequences from the fragment of (ii), which still retain the substantial activity. Applicants respectively disagree with this Examiner's assertion.

With the amendment to the claims, a modification of up to 5% of the 86 bp fragment permits only up to 4 bp mutations (i.e. 95% identity). As described below, one skilled in the art would have no difficulty at all identifying a series of sequences with such a small number of modifications that retain substantial activity of the promoter.

Applicants in general agree with the Examiner's logic that promoters often contain functionally-critical sequences. However, Applicants disagree with the Examiner's assertion that mutations of such sequences, more particularly by 1 to 4 bp, would render the promoter inactive. According to the prevailing model in the art, the promoter contains several nucleotide sequences where certain molecules essential for transcription can recognize and bind. Recruitment of some of such molecules (i.e. transcription factors) is essential for the promoter function; therefore, the nucleotide sequences recognized by these transcription factors are critical sequences. Numerous researches have found a variety of transcription factors and their specific recognition nucleotide sequences. For example, in the field of Plant Biology, more than 26,000 transcription factors from 22 plant species have been experimentally or computationally identified and their actual or presumptive DNA binding sequences have been revealed and publically available. (Gou et al., *Nucleic Acids Res.* 2008, 36:D966-969)

For purpose of instant illustration, some of known transcription factors and their recognition sites of are listed herein:

| Nucleotide Sequence | Transcription Factors |
|---|---|
| AGTTGGTTAAATAT | SBF-1 |
| GTCAGTTGGTTAA | MYB Ph3 |
| ACAGACCCG | P |
| GTTAATGACAC | DOF-2* |
| TGGGGCC | NTERF2 |

*(Note. The foregoing nucleotide sequences are collected from the publically available transcription factor binding sequence search websites, http://www.cbrc.jp/research/db /TFSEARCH.html and http://www.athamap.de/ if marked with *)*

The individual transcription factors listed above are usually non-substitutable to keep the transcription active, however, the recognition nucleotide sequences can be changed without significantly affecting their interaction with the transcription factors. According to Hao and the colleagues (*FEBS Letter*, 2003, 536:151-156), there are at least 33 variations of the "TGGGGCC" sequences (e.g. CGCCGCC, AGATGAC, AGCCGCC, CCGCCGAC, TGCCGGG and many others) that can still be recognized by NTERF2 factor when tested *in vitro*. This evidence indicates that several nucleotides of these critical regions can be modified without disrupting the functionality of the promoter. In light of this indication, Applicants believe that an isolated promoter of at least 95% identity to the 86 bp fragment of (ii) would still produce the claimed results.

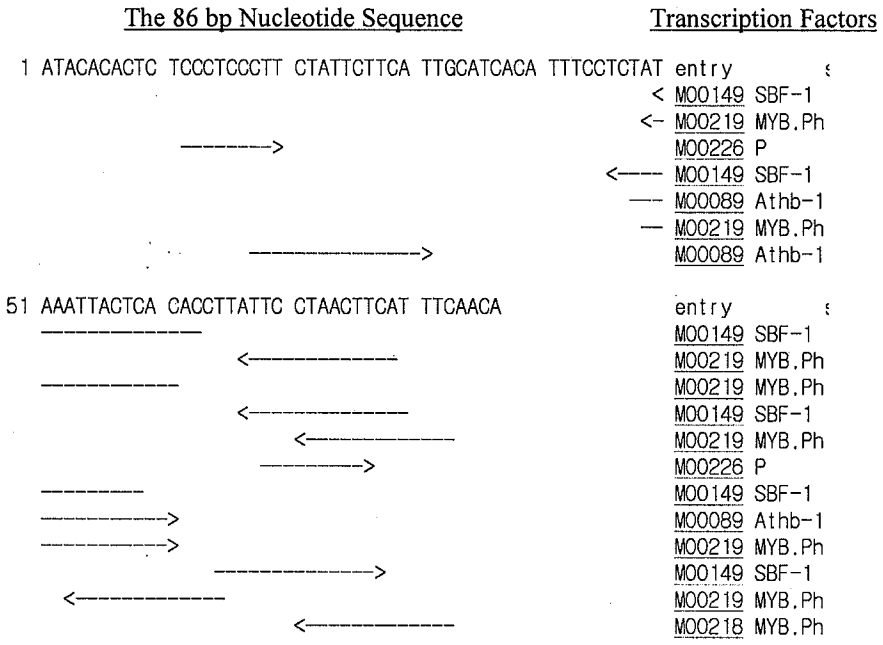
In addition, plant promoters are modular in nature, meaning that the specific activity of the promoter is typically due to small modular fragments within its sequence. These control sequences are normally separated by intervening DNA fragments that do not play important roles in determining the promoter activity and can be mutated without affecting the overall promoter activity. Even the modular fragments can be mutated to a certain degree without seriously affecting the overall promoter activity. This proves that mutations inside a promoter, in particular a plant gene promoter, are easy to perform while still retaining the promoter typical activity. Therefore, any researcher skilled in the art can perform random mutagenesis and as long as it does not interfere with one of the important promoter elements responsible for the observed activity it will render a promoter that is not identical to the initial one but still retain activity.

As described above, selection of specific nucleotides whose mutation may affect activity would not be necessary in order to enable the claimed subject matter. Nonetheless, if one with ordinary skill in the art would like to identify nucleotides that may least likely influence the promoter activity, the skilled person can perform routine experiments as disclosed in the specification or use other readily available tools in the art. For example, the skilled person can identify various sequences homologous to the 86 bp fragment of (ii) from related plant species as disclosed in claim 7. The routine experimental techniques in the art such as the nucleic acid hybridization and the cloning can be used to identify the homologous sequences. The homologous sequences, which show 95% or even less identity to the 86 bp, may be utilized to produce the claimed matters of claims 1, 7, and 15. Furthermore, once the homologous

sequences are found, the conserved nucleotides among the 86 bp would be recognized by another routine experimental tool such as nucleic acid sequencing. It is generally accepted in the field that the conservation is positively related to the functionality of the sequence. Therefore, the less conserved sequences out of 86 bp may be further selected for mutations to obtain the sequence variants cited in (iii) and (iv).

The specification also provides some other methods such as a serial deletion experiments to determine the functional sequence variants. As disclosed in Example 5 of the instant application, the skilled person can make a series of deletion mutants of the 86 bp (e.g. 10 bp deletion per mutant), and then tests these mutants for their promoter activity. These mutations and activity tests can also be done with routine techniques in the art such as the cloning, transformation and reporter assays. If one can find critical sequences that may affect the promoter activity, these critical sequences may not be mutated to produce claimed promoters of claims 1, 7, and 15.

In addition to the foregoing disclosed approaches to further determine the specific mutations, there are various techniques that are readily available to the skilled person in the art. For example, one can search for potential transcription binding sequences from the 86 bp fragment of (ii) using various publically available search tools. For an illustrative purpose, Applicants herein include the search result of potential transcription factor bindings to the 86 bp fragment which was obtained from http://www.cbrc.jp/htbin/nph-tfsearch.




*(Note. The arrow represents a potential recognition sequence of the corresponding transcription factor)*

According to this particular prediction result, nucleotides 1 to 11 or 32 to 45 would be least likely critical than other nucleotides as they may not be recognized by transcription factors. On the contrary, the skilled person would likely avoid mutating nucleotides 46 to 80 due to potential abundant recruitments. With such data available, one with ordinary skill in the art would make some educated guess and enable the claimed promoters with reasonable amount of experiments.

Another expressly available tool in the art is to observe the sequence conservation. It is generally accepted in the art that functionally important sequences would be less likely varied over the course of evolution. Therefore, searching for conserved sequences across the various species is one of very popular tool to find important genetic information. Such search is also practically convenient for any one with ordinary skill in the art using numerous public accessible online tools.

As well known in the art is a random mutagenesis experiment. Since the target sequence is fairly small, i.e. 86 bp in length, constructing a series of variants and testing them for their promoter activity is quite feasible. In particular, when coupled with the foregoing computational methods, the experimental determination of critical sequences should not be undue.

With the foregoing methods as well as other available methods in the art, one with ordinary skill in the art would be easily identify a sequence of 86 bp that is 95% or more identical to the sequence of (ii) and still retains the promoter activity.

As noted, there is a high level of predictability in the art that a substantial number of residues in the 86 bp fragment can be modified without affecting function. Therefore, the disclosure of every operable species should arguably not be required in this case as the specification provides an adequate basis to support the scope of the claims and the level of skill in the art at the priority date was clearly such that the skilled artisan would have a concrete expectation that they could readily identify and make the claimed functional sequences including the 86 bp fragment with up to 5% of residues (i.e. up to 4 residues) modified.. Furthermore, the methods of how to identify such operable species are disclosed in the specification and also are readily available in the art. Accordingly, Applicants believe the specification and claims provide the reasonable enablement of all the claimed subject matters, therefore, respectively request withdrawal of the rejection to claims 1, 7, and 15 under 35 U.S.C. § 112, first paragraph.

As to claims 9, 11-14 and 19-21, through their dependency from claim 1 or 7, they incorporate all the limitation of base claims. Therefore, they are also patentable for at least the same reasons that claims 1 and 7 are patentable as well as their own patentable features. Applicants respectively request reconsideration of these claims.

Claims 22-24 are canceled without prejudice. Therefore, the rejections to these claims are now moot.

**No Disclaimers or Disavowals**

Although the present communication may include alterations to the application or claims, or characterizations of claim scope or referenced art, Applicants are not conceding in this application that previously pending claims are not patentable over the cited references. Rather, any alterations or characterizations are being made to facilitate expeditious prosecution of this application. Applicants reserve the right to pursue at a later date any previously pending or other broader or narrower claims that capture any subject matter supported by the present disclosure, including subject matter found to be specifically disclaimed herein or by any prior prosecution. Accordingly, reviewers of this or any parent, child or related prosecution history shall not reasonably infer that Applicants have made any disclaimers or disavowals of any subject matter

supported by the present application.

## CONCLUSION

Applicants have endeavored to address all of the Examiner's concerns as expressed in the outstanding Office Action. Accordingly, arguments in support of the patentability of the pending claim set are presented above.

In light of the above remarks, reconsideration and withdrawal of the outstanding rejections is respectfully requested. If the Examiner has any questions which may be answered by telephone, he is invited to call the undersigned directly.

Please charge any additional fees, including any fees for additional extension of time, or credit overpayment to Deposit Account No. 11-1410.

Respectfully submitted,

KNOBBE, MARTENS, OLSON & BEAR, LLP

Dated: 3/24/09

By: 

Mark R. Benedict
Registration No. 44,531
Attorney of Record
Customer No. 20,995
(949) 760-0404

6811070_2
032409